2/16/05

```
=> s l1
SAMPLE SEARCH INITIATED 12:58:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      5 TO ITERATE

100.0% PROCESSED       5 ITERATIONS                                 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            5 TO      234
PROJECTED ANSWERS:               2 TO      124

L2            2 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 12:58:26 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    115 TO ITERATE

100.0% PROCESSED     115 ITERATIONS                               18 ANSWERS
SEARCH TIME: 00.00.01

L3           18 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               161.33     161.54

FILE 'CAPLUS' ENTERED AT 12:58:30 ON 16 FEB 2005
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FILE COVERS 1907 - 16 Feb 2005  VOL 142 ISS 8
FILE LAST UPDATED: 15 Feb 2005  (20050215/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            1 L3

=> d abs fbib hitstr
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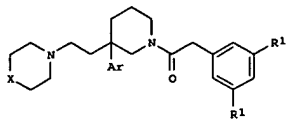
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
GI



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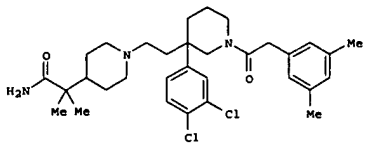

II

AB The invention relates to compds. I and their (in)organic acid salts, solvates and/or hydrates [wherein: X = NR2 or CHR2; Ar = Ph mono- or disubstituted by halo or C1-3 alkyl; R1 = Cl, Br, C1-3 alkyl, or CF3; R2 = CR3R4CONR5R6; R3, R4 = Me, Et, n-Pr, Bu; or CR3R4 forms C3-6 cycloalkyl; R5, R6 = H, C1-3 alkyl; or NR5R6 = azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, or perhydroazepin-1-yl]. The compds. exhibit a high affinity and high selectivity with respect to human NK1 receptors of substance P. The compds. are also orally active and demonstrate passage of the blood-brain barrier. The invention also relates to a method for production of I, intermediates useful in their production, pharmaceutical compns. containing them, and their use in the production of medicaments to treat all pathologies involving substance P and human NK1 receptors. Syntheses of 22 examples and a variety of intermediates are described. For instance, amidation of 3,5-dimethylphenylacetic acid with the (-)-isomer of 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)piperidine, followed by Swern oxidation of the alc. to an aldehyde, and reductive amination of this with 2-(piperidin-4-yl)isobutyramide-HCl, gave title compound (-)-II.HCl.H2O. Compds. I inhibited binding of substance P to human NK1 receptors in vitro with a Ki of approx. 10-11M, vs. 10-8M for NK2 receptors and 10-7 for NK3 receptors.

AN 2000:573786 CAPLUS

DN 133:177101

TI 1-[2-[1-(Phenylacetyl)-3-phenyl-3-piperidyl]ethyl]piperidine derivatives, method for the production thereof, and pharmaceutical compositions containing them as NK1 receptor antagonists

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IN Ducoux, Jean Philippe; Emonds-Alt, Xavier; Gueule, Patrick; Proietto, Vincenzo

PA Sanofi-Synthelabo, Fr.

SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000047572	A1	20000817	WO 2000-FR284	20000208
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			FR 1999-1593	A 19990210
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			WO 2000-FR284	W 20000208
BR 2000008067	A	20011106	BR 2000-8067	20000208
			FR 1999-1593	A 19990210
			FR 1999-4429	A 19990407
			WO 2000-FR284	W 20000208
EP 1150970	A1	20011107	EP 2000-903744	20000208
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TR 200102331	T2	20020321	TR 2001-200102331	20000208
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L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

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BG 105794	A	20020531	BG 2001-105794	20010808
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			WO 2000-FR284	W 20000208
US 6642233	B1	20031104	US 2001-913106	20010809
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			FR 1999-4429	A 19990407
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US 2004072840	A1	20040415	US 2003-663124	20030916
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			FR 1999-4429	A 19990407
			WO 2000-FR284	W 20000208
			US 2001-913106	A3 20010809

OS MARPAT 133:177101

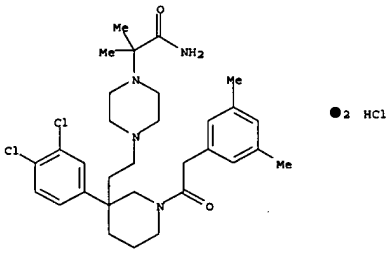
IT **288378-97-2P 288378-98-3P 288379-04-4P**
288379-06-6P 288379-08-8P 288379-10-2P
288379-14-6P 288379-22-6P 288379-26-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of [[(phenylacetyl)phenylpiperidyl]ethyl]piperidine derivs. as NK1 receptor antagonists)

RN 288378-97-2 CAPLUS

CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dimethylphenyl)acetyl]-3-piperidinyl]ethyl]-α,α-dimethyl-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 288378-98-3 CAPLUS

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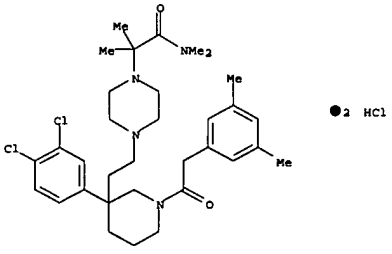
Rotation (-).

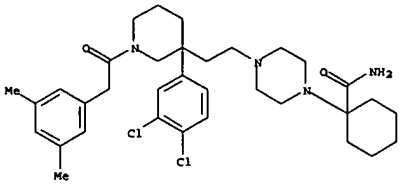


RN 288379-04-4 CAPLUS

CN Cyclohexanecarboxamide, 1-[4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dimethylphenyl)acetyl]-3-piperidinyl]ethyl]-1-piperazinyl]-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

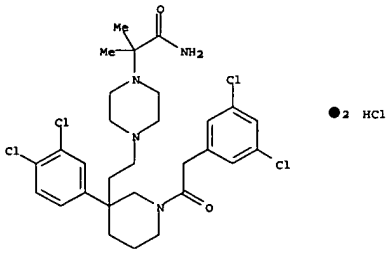
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

RN 288379-06-6 CAPLUS
CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dichlorophenyl)acetyl]-3-piperidinyl]ethyl]-α,α-dimethyl-, dihydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

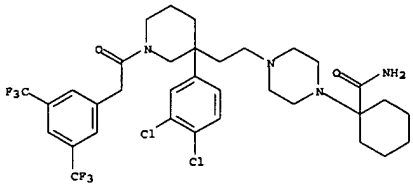


●2 HCl

RN 288379-08-8 CAPLUS
CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dichlorophenyl)acetyl]-3-piperidinyl]ethyl]-N,N,α,α-tetramethyl-, dihydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

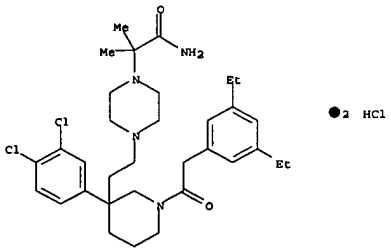
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

RN 288379-22-6 CAPLUS
CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-diethylphenyl)acetyl]-3-piperidinyl]ethyl]-α,α-dimethyl-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

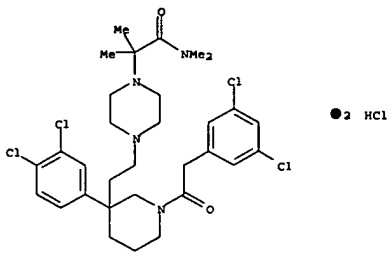
Rotation (-).



●2 HCl

RN 288379-26-0 CAPLUS
CN 1-Piperazineacetamide, 4-[2-[1-[(3,5-dichlorophenyl)acetyl]-3-(3,4-dimethylphenyl)-3-piperidinyl]ethyl]-α,α-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

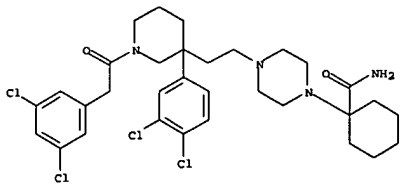
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

RN 288379-10-2 CAPLUS
CN Cyclohexanecarboxamide, 1-[4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dichlorophenyl)acetyl]-3-piperidinyl]ethyl]-1-piperazinyl]-, dihydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

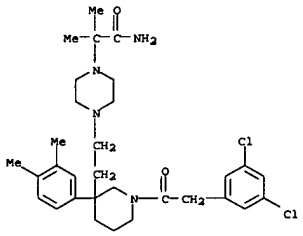


●2 HCl

RN 288379-14-6 CAPLUS
CN Cyclohexanecarboxamide, 1-[4-[2-[1-[[3,5-bis(trifluoromethyl)phenyl]acetyl]-3-(3,4-dichlorophenyl)-3-piperidinyl]ethyl]-1-piperazinyl]-, dihydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



●2 HCl

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

2/16/05

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

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